

HIGH PRODUCTION VOLUME (HPV)
CHEMICAL CHALLENGE PROGRAM

TEST PLAN

For

4,4'-Bis(alpha, alpha-dimethylbenzyl)diphenylamine

CAS No. 10081-67-1

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Submitted to the US EPA
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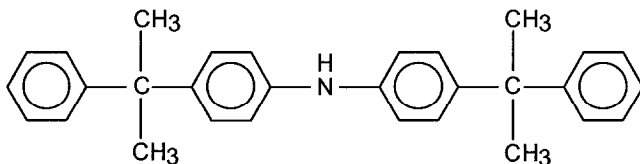
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1. General Information

1.1 CAS Number: 10081-67-1

1.2 Molecular Weight: 405.59

1.3 Structure and formula: $C_{30}H_{31}N$



1.4 Introduction

4,4'-Bis(alpha, alpha-dimethylbenzyl)diphenylamine is an antioxidant, used as a thermal stabiliser in the plastics industry (including specific uses in the production of polyolefins, styrenics, polyols, hot melt adhesives, lubricants and polyamines).

2. Review of Existing Data and Development of Test Plan

Crompton Corporation has undertaken a comprehensive evaluation of all relevant data on the SIDS endpoints of concern for 4,4'-bis(alpha, alpha-dimethylbenzyl)diphenylamine.

The availability of the data on the specific SIDS endpoints is summarized in Table 1. Table 1 also shows data gaps that will be filled by additional testing.

Table 1: Available adequate data and proposed testing on 4,4'-bis(alpha,alpha-dimethylbenzyl)diphenylamine

CAS No. 10081-67-1	Information Available?	GLP	OECD Study?	Other Study?	Estimation Method?	Acceptable?	SIDS Testing required?
	Y/N	Y/N	Y/N	Y/N	Y/N	Y/N	Y/N
Physicochemical							
Melting Point	Y						N
Boiling Point	Y				Y	Y	N
Vapour Pressure	Y	N		Y		Y	N
Water Solubility	Y	N		Y		Y	N
Partition Coefficient (Kow)	Y				Y	Y	N
Environmental Fate							
Biodegradation	Y				Y	Y	N
Hydrolysis	N						N
Photodegradation	Y				Y	Y	N
Transport and Distribution between Environmental Compartments	Y				Y	Y	N
Ecotoxicology							
Acute Fish	Y				Y	Y	N
Acute Daphnia	Y				Y	Y	N
Acute Algae	Y				Y	Y	N
Toxicology							
Acute Oral	Y			Y		Y	N
Repeat Dose toxicity	N						Y
Genetic toxicity – Gene mutation	Y			Y		Y	N
Genetic toxicity – Chromosome aberration	N						Y
Reproductive toxicity	N						Y
Developmental toxicity/teratogenicity	N						Y

A. Evaluation of Existing Physicochemical Data and Proposed Testing

1. Melting Point

The Safety Data Sheet for 4,4'-bis(alpha, alpha-dimethylbenzyl)diphenylamine quotes a melting point of 95°C.

2. Boiling Point

The Safety Data Sheet for 4,4'-bis(alpha, alpha-dimethylbenzyl)diphenylamine reports an autoflammability temperature of 298°C. This suggests that the substance will not reach the boiling temperature, calculated to be 507.8 °C using MPBPWIN v1.40.

3. Vapour Pressure

The vapour pressure of 4,4'-bis(alpha, alpha-dimethylbenzyl)diphenylamine was measured to be 6.67 hPa at 20°C using a method similar to OECD Method 104.

4. Water Solubility

The water solubility of 4,4'-bis(alpha, alpha-dimethylbenzyl)diphenylamine was measured to be 7 mg/L.

5. Partition Coefficient

The partition coefficient (i.e. Kow) for 4,4'-bis(alpha, alpha-dimethylbenzyl)diphenylamine was calculated as log Kow = 8.51 using KOWWIN v1.66.

Summary of Physicochemical Properties Testing: Existing data for melting point, boiling point, vapour pressure, partition coefficient and water solubility are considered to fill these endpoints adequately.

B. Evaluation of Existing Environmental Fate Data and Proposed Testing

1. Biodegradation

The biodegradability of the chemical has been estimated using Biowin v4.00 and the results indicate the chemical not to be readily biodegradable.

2. Hydrolysis

There are no hydrolysable groups in the chemical structure, and the substance is predicted to be hydrolytically stable. In addition, hydrolysis testing of poorly soluble substances (i.e. solubility <10 mg/l) is technically difficult. Therefore, no testing will be performed to fulfill this endpoint.

3. Photodegradation

The potential for photodegradation of 4,4'-bis(alpha, alpha-dimethylbenzyl) diphenylamine has been estimated using the AOPWIN v1.90, and indicated atmospheric oxidation via OH radicals reaction with a half-life of 0.64 hours.

4. Transport and Distribution between Environmental Compartments

An Epiwin Level III Fugacity Model calculation has been conducted for 4,4'-bis(alpha, alpha-dimethylbenzyl)diphenylamine and indicates distribution mainly to sediment for emissions of 1000 kg/hr simultaneously to air water and soil compartments.

Summary of Environmental Fate Testing: Existing data for photodegradation and transport and distribution between environmental compartments are considered to fill these endpoints

adequately. The chemical contains no hydrolysable or biodegradable groups, therefore no hydrolysis or biodegradation testing is proposed.

C. Evaluation of Existing Ecotoxicity Data and Proposed Testing

1. Acute Toxicity to Fish

Estimation using ECOSAR v0.99g gives an LC_{50} (96 h) of 0.00023 mg/L.

2. Acute Toxicity to Algae

Estimation using ECOSAR v0.99g gives an LC_{50} (96 h) of 0.000349 mg/L.

3. Acute Toxicity to Daphnia

Estimation using ECOSAR v0.99g gives an LC_{50} (48 h) of 0.00038 mg/L.

Summary of Ecotoxicity Testing: The chemical belongs to the Ecosar class of neutral organics. The predicted values for acute toxicity to fish, daphnia and algae are regarded as being valid for this material and no testing is proposed.

D. Evaluation of Existing Human Health Effects Data and Proposed Testing

1. Acute Oral Toxicity

The acute oral toxicity has been determined (similar to OECD 401, rat, non-GLP), with a reported LD50 value of > 10,000 mg/kg b.w. Data from a closely related analogue of the sponsored chemical (styrenated N-phenyl-benzenamine, CAS # 68442-68-2) indicates an oral LD50 >500 - >20,000 mg/kg. It is proposed that read across from this analogue is valid and reduces concern over the acute toxicity of 4,4'-bis(alpha,alpha-dimethylbenzyl)diphenylamine, therefore no further testing will be performed.

2. Skin Irritation

This non-SIDS endpoint has been evaluated (similar to OECD 404, rabbit, non-GLP). The substance was not classified as irritating to skin.

3. Eye Irritation

This non-SIDS endpoint has been evaluated (rabbit, non-GLP). The substance was not classified as an eye irritant.

4. Repeat Dose Toxicity

The repeat dose toxicity of 4,4'-bis(alpha,alpha-dimethylbenzyl)diphenylamine will be determined using OECD Method 422.

5. Genotoxicity

4,4'-Bis(alpha,alpha-dimethylbenzyl)diphenylamine was determined to be non-mutagenic in an Ames reverse mutation assay (Ames test, *S. typhimurium* strains TA98, TA100, TA1535, TA1537, TA1538, GLP).

The *in vitro* cytogenicity of 4,4'-bis(alpha,alpha-dimethylbenzyl)diphenylamine will be determined using OECD Method 473.

6. Reproductive and Developmental Toxicity

The developmental and reproductive toxicity of 4,4'-bis(alpha,alpha-dimethylbenzyl)diphenylamine in rat will be determined using OECD Method 422.

Summary of Human Health Effects Testing: The repeat dose toxicity combined with the developmental and reproductive toxicity will be evaluated using OECD Method 422. The potential to cause *in vitro* chromosomal aberrations will be determined using OECD Method 473. The existing data for acute oral toxicity and mutagenicity in a bacterial system are considered to fulfil these endpoints adequately and no further testing will be undertaken. 4,4'-Bis(alpha, alpha-dimethylbenzyl)diphenylamine has been shown to be neither a skin nor an eye irritant.

3. Evaluation of Data for Quality and Acceptability

The collected data were reviewed for quality and acceptability following the general US EPA guidance [2] and the systematic approach described by Klimisch et al [3]. These methods include consideration of the reliability, relevance and adequacy of the data in evaluating their usefulness for hazard assessment purposes. This scoring system was only applied to ecotoxicology and human health endpoint studies per EPA recommendation [4]. The codification described by Klimisch specifies four categories of reliability for describing data adequacy. These are:

- (1) **Reliable without restriction:** Includes studies or data complying with Good Laboratory Practice (GLP) procedures, or with valid and/or internationally accepted testing guidelines, or in which the test parameters are documented and comparable to these guidelines.
- (2) **Reliable with Restrictions:** Includes studies or data in which test parameters are documented but vary slightly from testing guidelines.
- (3) **Not Reliable:** Includes studies or data in which there are interferences, or that use non-relevant organisms or exposure routes, or which were carried out using unacceptable methods, or where documentation is insufficient.
- (4) **Not Assignable:** Includes studies or data in which insufficient detail is reported to assign a rating, e.g. listed in abstracts or secondary literature.

4. References

- [1] US EPA, EPI Suite Software, 2000
- [2] USEPA (1998). Guidance for Meeting the SIDS Requirements (The SIDS Guide). Guidance for the HPV Challenge Program. Dated 11/2/98.
- [3] Klimisch, H.-J., et al (1997). A Systematic Approach for Evaluating the Quality of Experimental Toxicological and Ecotoxicological Data. Regul. Toxicol. Pharmacol. 25:1-5
- [4] USEPA (1999). Determining the Adequacy of Existing Data. Guidance for the HPV Challenge Program. Draft dated 2/10/99.